

REMARKS

As an initial matter, Applicants wish to thank the Examiner for indicating that Claims 8-11, 13-15 and 25-31 are allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 2-31 and 33-35 are pending in this application. Claims 2, 16, 22, 23, 28, 29, and 33 have been amended. In particular, Claims 2, 16, 28, and 29 have been amended to correct typographical errors and grammatical errors, such as missing commas and hyphens, as well as an incorrect formula (Claim 2). In addition, it is noted that Claim 16 in the Preliminary Amendment filed on January 11, 2002 contains inconsistencies between that shown in Appendix A labeled "Version with Markings to show Changes Made" with that shown in the Response section. In amending Claim 16, the present Amendment and Response uses Claim 16 shown in the Response section of the Preliminary Amendment. Upon entry of this Amendment, claims 2-16, 22-31 and 33-35 will be pending in this application.

Attached hereto as Appendix A captioned "Version with Markings to show changes made" is a marked-up version of the changes made to the claims by the current amendment. In addition, for the convenience of the Examiner, all claims now pending following entry of the present Amendment and Response are reproduced in Appendix B captioned "Pending Claims."

Claim 33

Claim 33 has been amended *inter alia* by replacing "cycloakoxy" with "cyclyloxy" as suggested by the Examiner.

Double Patenting

Claims 2-6, 16, 22-24, and 33-35 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 19-21 of U.S. Patent No. 6,376,527.

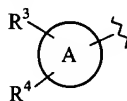
When appropriate, Applicants will file a terminal disclaimer to overcome this double patenting rejection. However, at this time, Applicants request this issue be deferred until all of the other outstanding issues have been resolved.

Rejection under 35 U.S.C. §103

Claims 2-7, 12, 16-24, and 33-35 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the Faraci reference (WO 94/13643).

Specifically, the Examiner asserts that the compounds of the present invention are embraced by the generic description of the compound in the Faraci reference. As discussed in detail below, as amended the generic compound disclosed in the Faraci reference does not encompass the compounds of the present invention; therefore, the rejection of claims under 35 U.S.C. §103(a) should be withdrawn.

The substituent that corresponds to a moiety of the formula:



in Compound of Formula I of the present invention is “R³” in the Faraci reference. This “R³” in the Faraci reference is defined as:

...phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinolyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzoisothiazolyl, thiazolyl, isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl, azaindolyl, benzoxazolyl, oxazolyl, pyrrolidinyl, thiazolidinyl, morpholinyl, pyridinyl, tetrazolyl, or 9 to 12 membered bicycloalkyl, optionally containing one to three of O, S or N-Z wherein Z is hydrogen, C₁-C₄ alkyl, C₁-C₄ alkanoyl, phenyl or phenylmethyl, wherein each one of the above groups may be substituted independently by from one to three of fluoro, chloro, bromo, C₁-C₆ alkyl, C₁-C₆ alkoxy, or trifluoromethyl, or one of cyano, nitro, amino, NH(C₁-C₆ alkyl), N(C₁-C₄ alkyl)(C₁-C₂ alkyl), COO(C₁-C₄ alkyl), CO(C₁-C₄ alkyl), SO₂NH(C₁-C₄ alkyl), SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), SO₂NH₂, NHSO₂(C₁-C₄ alkyl), S(C₁-C₆ alkyl), SO₂(C₁-C₆ alkyl), wherein alkyl and C₁-C₆ alkyl may be substituted by one or two of fluoro, chloro, hydroxy, amino, methylamino, dimethylamino or acetyl[.]

Page 2, lines 12-24. Therefore, the possible substituents for where R₃ is phenyl in the Faraci reference are limited to:

...one to three of fluoro, chloro, bromo, C₁-C₆ alkyl, C₁-C₆ alkoxy, or trifluoromethyl, or one of cyano, nitro, amino, NH(C₁-C₆ alkyl), N(C₁-C₄ alkyl)(C₁-C₂ alkyl), COO(C₁-C₄ alkyl), CO(C₁-C₄ alkyl), SO₂NH(C₁-C₄ alkyl), SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), SO₂NH₂,

NHSO₂(C₁-C₄ alkyl), S(C₁-C₆ alkyl), SO₂(C₁-C₆ alkyl), wherein alkyl and C₁-C₆ alkyl may be substituted by one or two of fluoro, chloro, hydroxy, amino, methylamino, dimethylamino or acetyl[.]

Page 2, lines 19-24.

In contrast, the possible substituents (i.e., R³) for aryl group "A" of the present invention are:

- (a) acylamino;
- (b) optionally substituted heterocyclyl;
- (c) optionally substituted aryl or heteroaryl;
- (d) heteroalkenyl;
- (e) heteroalkynyl;
- (f) heteroalkoxy;
- (g) optionally substituted heterocyclylalkyl;
- (h) optionally substituted heterocyclylalkenyl;
- (i) optionally substituted heterocyclylalkynyl;
- (j) optionally substituted heterocyclylalkoxy, cyclyloxy, or heterocycloxy;
- (k) optionally substituted heterocyclylalkylamino;
- (l) optionally substituted heterocyclylalkylcarbonyl;
- (m) -NHSO₂R⁶ where R⁶ is optionally substituted heterocyclylalkyl;
- (n) -NHSO₂NR⁷R⁸ where R⁷ and R⁸ are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (o) -Y-(alkylene)-R⁹ where:

Y is a single bond, -O-, -NH- or -S(O)_n- (where n is an integer from 0 to 2); and R⁹ is cyano, optionally substituted heteroaryl, -COOH, -COR¹⁰, -COOR¹¹, -CONR¹²R¹³, -SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹, where R¹⁰ is optionally substituted heterocycle, R¹¹ is alkyl, and R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are, independently of each other, hydrogen, alkyl or heteroalkyl;

- (p) $-C(=NR^{20})(NR^{21}R^{22})$ where R^{20} , R^{21} and R^{22} independently represent hydrogen, alkyl or hydroxy, or R^{20} and R^{21} together are $-(CH_2)_n-$ where n is 2 or 3 and R^{22} is hydrogen or alkyl;
- (q) $-NHC(=X)NR^{23}R^{24}$ where X is O or S, and R^{23} and R^{24} are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (r) $-CONR^{25}R^{26}$ where R^{25} and R^{26} independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclalkyl, or R^{25} and R^{26} together with the nitrogen to which they are attached form an optionally substituted heterocycl ring;
- (s) $-S(O)_nR^{27}$ where n is an integer from 0 to 2, and R^{27} is optionally substituted heterocyclalkyl;
- (t) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;
- (u) arylaminoalkylene or heteroarylaminoalkylene;
- (v) Z-alkylene- $NR^{30}R^{31}$ or Z-alkylene- OR^{32} where Z is -O-, and R^{30} , R^{31} and R^{32} are independently of each other, hydrogen, alkyl or heteroalkyl;
- (w) $-OC(O)$ -alkylene- CO_2H or $-OC(O)-NR'R''$ (where R' and R'' are independently hydrogen or alkyl); and
- (x) heteroarylalkenylene or heteroarylalkynylene.

The differences between the substituents R^3 of the present invention and the substituents on the phenyl ring R_3 of the Faraci reference are shown in the substituent comparison Table below.

Substituent Comparison Table

Possible R_3 Substituent(s) on the Phenyl group of the Faraci reference ¹	Substituent R^3 on the Aryl group "A" of the present invention
one to three of	
fluoro, chloro, bromo,	No halide is claimed. Therefore, there is no overlap with the compounds discussed in the Faraci reference.
C_1 - C_6 alkyl, C_1 - C_6 alkoxy, or trifluoromethyl,	No alkyl, alkoxy, or trifluoromethyl is claimed. Alkyl groups of R^3 in the present invention are substituted with optionally substituted heterocycl (see (g) above), cycloalkyl (see (t) above), etc. Therefore, there is no

	overlap with the compounds discussed in the Faraci reference.
or one of cyano,	In the present invention, cyano group is present in -Y-(alkylene)-R ⁹ form where: Y is a single bond, -O-, -NH- or -S(O) _n - (where n is an integer from 0 to 2); and R ⁹ is cyano.... Therefore, a simple cyano group on the aryl group is <u>NOT</u> claimed in the present invention, i.e., unlike the compounds discussed in the Faraci reference, when the cyano group is present in the present invention, an alkylene chain between the cyano group and the aryl group is also present. Therefore, there is no overlap with the compounds discussed in the Faraci reference.
nitro,	No nitro group is claimed. Therefore, there is no overlap with the compounds discussed in the Faraci reference.
amino,	No amino group is claimed. Therefore, there is no overlap with the compounds discussed in the Faraci reference.
NH(C ₁ -C ₆ alkyl), N(C ₁ -C ₄ alkyl)(C ₁ -C ₂ alkyl),	No alkyl amino or dialkyl amino group is claimed. Some of the amino groups claimed in the present invention are non-alkyl or non-dialkyl amino groups such as acylamino (see (a) above); and optionally substituted heterocyclylalkylamino (see (k) above). Therefore, there is no overlap with the compounds discussed in the Faraci reference.
COO(C ₁ -C ₄ alkyl),	This type of substituent is not claimed in the present invention. Therefore, there is no overlap with the compounds discussed in the Faraci reference.
CO(C ₁ -C ₄ alkyl),	Alkyl carbonyl substituent is not claimed in the present invention. R ³ of the present invention include heterocyclylalkylcarbonyl (see (l) above); therefore, unlike the compounds in the Faraci reference, the alkyl group in this carbonyl group is substituted with heterocyclyl group. Therefore, there is no overlap with the compounds discussed in the Faraci reference.
SO ₂ NH(C ₁ -C ₄ alkyl), SO ₂ N(C ₁ -C ₄ alkyl)(C ₁ -C ₂ alkyl), SO ₂ NH ₂ ,	R ³ of the present invention can be -S(O) _n R ²⁷ where n is an integer from 0 to 2. However, R ²⁷ is optionally substituted heterocyclylalkyl. See (s) above. Therefore, there is no overlap with the compounds discussed in the Faraci reference.
NHSO ₂ (C ₁ -C ₄ alkyl),	R ³ of the present invention can be -NHSO ₂ R ⁶ . However, R ⁶ is optionally substituted heterocyclylalkyl. See (m) above. Therefore, R ⁶ can not be an alkyl group. Accordingly, there is no overlap with the compounds

	discussed in the Faraci reference.
S(C ₁ -C ₆ alkyl), SO ₂ (C ₁ -C ₆ alkyl),	R ³ of the present invention can be -S(O) _n R ²⁷ where n is an integer from 0 to 2. However, R ²⁷ is optionally substituted heterocyclalkyl. See (s) above. Thus, R ²⁷ can not be an alkyl group. Therefore, there is no overlap with the compounds discussed in the Faraci reference.
wherein alkyl and C ₁ -C ₆ alkyl may be substituted by one or two of fluoro, chloro, hydroxy, amino, methylamino, dimethylamino or acetyl[.]	Even with this expanded definition of the C ₁ -C ₆ alkyl in the Faraci reference, there is no overlap between the compounds of the present invention and the compounds discussed in the Faraci reference.

1. See page 2, lines 19-24 of the Faraci reference.

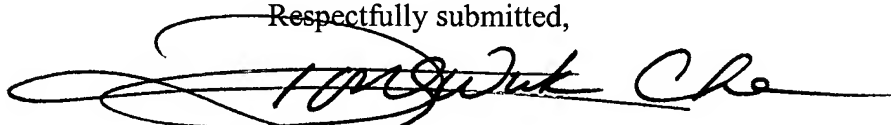
As shown in the substituent comparison Table above, as amended none of the R³ substituents of the present invention overlaps with the generic concept disclosed in the Faraci reference. Accordingly, Applicants request withdrawal of the rejection under 35 U.S.C. §103(a).

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,



Don D. Cha
Reg. No. 40,945

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (303) 571-4000
Fax: (303) 571-4321
DDC:bhr
DE 7073924 v1

APPENDIX A
VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 17-21 have been cancelled.

Claims 2, 16, 22, 23, 28, 29, and 33 have been amended as follows.

2. (Amended Herein) The method of Claim 33 wherein R³ is:
- (a) optionally substituted heterocyclyl;
 - (b) aryl or heteroaryl both optionally substituted with a substituent selected from halo, alkyl, amino, alkoxy, carboxy, lower alkoxy carbonyl, SO₂R' (where R' is alkyl) or ~~SO₂NHR'R''~~ SO₂NR'R'' (where R' and R'' are independently hydrogen or alkyl);
 - (c) heteroalkyl;
 - (d) heteroalkenyl;
 - ~~(e) heteroalkylamino;~~
 - ~~(f)~~ (e) heteroalkoxy;
 - ~~(g)~~ (f) optionally substituted heterocyclylalkyl or heterocyclylalkoxy;
 - ~~(h)~~ (g) optionally substituted heterocyclylalkenyl;
 - ~~(i)~~ (h) optionally substituted heterocyclylalkynyl;
 - ~~(j)~~ (i) optionally substituted heterocyclylalkoxy;
 - ~~(k)~~ (j) optionally substituted heterocyclylalkylamino;
 - ~~(l)~~ (k) optionally substituted heterocyclylalkylcarbonyl;
 - ~~(m)~~ (l) -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted heteroaryl, -CONR¹²R¹³, -SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl;
 - ~~(n)~~ (m) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;

- ~~(m)~~ (n) arylaminoalkylene or heteroarylaminomalkylene; or
~~(n)~~ (o) Z-alkylene-NR³⁰R³¹ where Z is -NH-, -N(alkyl)- or -O-, and R³⁰ and R³¹ are independently of each other, hydrogen, alkyl or heteroalkyl.

16. (Amended Herein) The method of Claim 5, wherein R³ is:

- (a) heteroalkyl;
- (b) heteroalkoxy;
- ~~(c) heteroalkylamino;~~
- ~~(d)~~ (c) optionally substituted heterocyclalkyl;
- ~~(e)~~ (d) optionally substituted heterocyclalkoxy;
- ~~(f)~~ (e) optionally substituted heterocyclalkylamino;
- ~~(g)~~ (f) -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted heteroaryl, -CONR¹²R¹³, SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl; or
- ~~(h)~~ (g) Z-alkylene-NR³⁰R³¹ where Z is -NH-, -N(alkyl)- or -O-, and R³⁰ and R³¹ are independently of each other, hydrogen, alkyl or heteroalkyl.

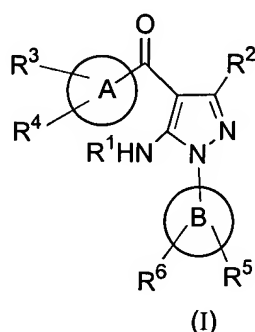
22. (Amended Herein) The method of Claim 16, wherein R³ is heteroalkoxy ~~or heteroalkylamino~~.

23. (Amended Herein) The method of Claim 22, wherein R³ is at the 3-position and is selected from the group consisting of 3-dimethylaminopropoxy, 2-dimethylaminoethoxy, 2-hydroxyethoxy, 2,3-dihydroxypropoxy, and 2,2-(dihydroxymethyl)ethoxy, ~~2-dimethylaminoethylamino and 3-dimethylaminopropylamino~~.

28. (Amended Herein) The method of Claim 16 wherein R³ is -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted heteroaryl, -CONR¹²R¹³, -SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl.

29. (Amended Herein) The method of Claim 28, wherein Y is a single bond and R⁹ is -SO₂R¹⁴ or -SO₂NR¹⁵R¹⁶.

33. (Amended Herein) A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a therapeutically effective amount of a compound selected from the group of compounds represented by Formula (I):



wherein:

R¹ is hydrogen or acyl;

R² is hydrogen or alkyl;

A is an aryl ring;

B is an aryl ring;

R³ is selected from the group consisting of:

- (a) ~~amino, alkylamino or dialkylamino;~~
- ~~(b)~~ (b) acylamino;
- ~~(c)~~ (b) optionally substituted heterocyclyl;
- ~~(d)~~ (c) optionally substituted aryl or heteroaryl;
- ~~(e)~~ ~~heteroalkyl;~~
- ~~(f)~~ (d) heteroalkenyl;
- ~~(g)~~ (e) heteroalkynyl;
- ~~(h)~~ (f) heteroalkoxy;
- ~~(i)~~ ~~heteroalkylamino;~~
- ~~(j)~~ (g) optionally substituted heterocyclalkyl;

- ~~(h)~~ **(h)** optionally substituted heterocyclalkenyl;
- ~~(i)~~ **(i)** optionally substituted heterocyclalkynyl;
- ~~(m)~~ **(j)** optionally substituted heterocyclalkoxy, ~~cycloalkoxy~~ **cyclioxy**,
or ~~heterocycloxy~~ **heterocyclioxy**;
- ~~(n)~~ **(k)** optionally substituted heterocyclalkylamino;
- ~~(o)~~ **(l)** optionally substituted heterocyclalkylcarbonyl;
- ~~(p)~~ ~~heteroalkylcarbonyl~~;
- ~~(q)~~ **(m)** -NHSO₂R⁶ where R⁶ is ~~alkyl, heteroalkyl or~~ optionally
substituted heterocyclalkyl;
- ~~(r)~~ **(n)** -NHSO₂NR⁷R⁸ where R⁷ and R⁸ are, independently of each other,
hydrogen, alkyl or heteroalkyl;
- ~~(s)~~ **(o)** -Y-(alkylene)-R⁹ where:
Y is a single bond, -O-, -NH- or -S(O)_n- (where n is an integer
from 0 to 2); and R⁹ is cyano, optionally substituted heteroaryl, -
COOH, -COR¹⁰, -COOR¹¹, -CONR¹²R¹³, -SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -
NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹, where R¹⁰ is ~~alkyl or~~
substituted heterocycle, R¹¹ is alkyl, and R¹², R¹³, R¹⁴, R¹⁵, R¹⁶,
R¹⁷, R¹⁸ and R¹⁹ are, independently of each other, hydrogen, alkyl
or heteroalkyl;
- ~~(t)~~ **(p)** -C(=NR²⁰)(NR²¹R²²) where R²⁰, R²¹ and R²² independently
represent hydrogen, alkyl or hydroxy, or R²⁰ and R²¹ together are -
(CH₂)_n- where n is 2 or 3 and R²² is hydrogen or alkyl;
- ~~(u)~~ **(q)** -NHC(=X)NR²³R²⁴ where X is ~~O or S~~ **O or S**, and R²³ and R²⁴
are, independently of each other, hydrogen, alkyl or heteroalkyl;
- ~~(v)~~ **(r)** -CONR²⁵R²⁶ where R²⁵ and R²⁶ independently represent hydrogen,
alkyl, heteroalkyl or optionally substituted heterocyclalkyl, or
R²⁵ and R²⁶ together with the nitrogen to which they are attached
form an optionally substituted heterocycl ring;

- ~~(w)~~ (s) $-S(O)_nR^{27}$ where n is an integer from 0 to 2, and R^{27} is ~~alkyl,~~
~~heteroalkyl,~~ optionally substituted heterocyclalkyl, ~~or $-NR^{28}R^{29}$~~
~~where R^{28} and R^{29} are, independently of each other, hydrogen,~~
~~alkyl or heteroalkyl;~~
- ~~(t)~~ (t) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all
optionally substituted with alkyl, halo, hydroxy or amino;
- ~~(u)~~ (u) arylaminoalkylene or heteroarylaminomethylene;
- ~~(v)~~ (v) Z-alkylene- $NR^{30}R^{31}$ or Z-alkylene- OR^{32} where Z is ~~$-NH-$~~
 ~~$N(lower\ alkyl)-$ or $-O-$~~ , and R^{30} , R^{31} and R^{32} are independently of
each other, hydrogen, alkyl or heteroalkyl;
- ~~(aa)~~ (w) $-OC(O)-alkylene-CO_2H$ or $-OC(O)-NR'R''$ (where R' and
 R'' are independently hydrogen or alkyl); and
- ~~(bb)~~ (x) heteroarylalkenylene or heteroarylalkynylene;

R^4 is selected from the group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) alkoxy; and
- (e) hydroxy;

R^5 is selected from the group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) haloalkyl;
- (e) thioalkyl;
- (f) hydroxy;
- (g) amino;
- (h) alkylamino;
- (i) dialkylamino;

- (j) heteroalkyl;
- (k) optionally substituted heterocycle;
- (l) optionally substituted heterocyclalkyl;
- (m) optionally substituted heterocyclalkoxy;
- (n) alkylsulfonyl;
- (o) aminosulfonyl, mono-alkylaminosulfonyl or dialkylaminosulfonyl;
- (p) heteroalkoxy; and
- (q) carboxy;

R⁶ is selected from a group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl; and
- (d) alkoxy; and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

APPENDIX B
PENDING CLAIMS

2. (Amended Herein) The method of Claim 33 wherein R³ is:
- (a) optionally substituted heterocyclyl;
 - (b) aryl or heteroaryl both optionally substituted with a substituent selected from halo, alkyl, amino, alkoxy, carboxy, lower alkoxy carbonyl, SO₂R' (where R' is alkyl) or SO₂NR'R'' (where R' and R'' are independently hydrogen or alkyl);
 - (c) heteroalkyl;
 - (d) heteroalkenyl;
 - (e) heteroalkoxy;
 - (f) optionally substituted heterocyclylalkyl or heterocycliloxy;
 - (g) optionally substituted heterocyclylalkenyl;
 - (h) optionally substituted heterocyclylalkynyl;
 - (i) optionally substituted heterocyclylalkoxy;
 - (j) optionally substituted heterocyclylalkylamino;
 - (k) optionally substituted heterocyclylalkylcarbonyl;
 - (l) -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted heteroaryl, -CONR¹²R¹³, -SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl;
 - (m) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;
 - (n) arylaminoalkylene or heteroarylaminoalkylene; or
 - (o) Z-alkylene-NR³⁰R³¹ where Z is -NH-, -N(alkyl)- or -O-, and R³⁰ and R³¹ are independently of each other, hydrogen, alkyl or heteroalkyl.
3. The method of Claim 2 wherein R¹ and R² are hydrogen; and B is phenyl.

4. The method of Claim 3 wherein A is phenyl.
5. The method of Claim 4 wherein R^4 is hydrogen; and R^5 is halo or alkyl.
6. The method of Claim 5 wherein R^5 is chloro, fluoro or methyl; and R^6 is hydrogen, chloro, fluoro, methyl or methoxy.
7. The method of Claim 5, wherein R^3 is optionally substituted heteroaryl.
8. The method of Claim 7, wherein R^3 is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted.
9. The method of Claim 8, wherein R^3 is at the 3-position.
10. The method of Claim 9, wherein R^5 is 4-F and R^6 is hydrogen.
11. The method of Claim 9, wherein R^5 is 2-Me and R^6 is hydrogen.
12. The method of Claim 5, wherein R^3 is optionally substituted phenyl.
13. The method of Claim 12, wherein R^3 is 3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl.
14. The method of Claim 13, wherein R^3 is at the 3-position.
15. The method of Claim 14, wherein R^5 is 4-F and R^6 is hydrogen.
16. (Amended Herein) The method of Claim 5, wherein R^3 is:
 - (a) heteroalkyl;
 - (b) heteroalkoxy;
 - (c) optionally substituted heterocyclalkyl;
 - (d) optionally substituted heterocyclalkoxy;
 - (e) optionally substituted heterocyclalkylamino;

- (f) -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted heteroaryl, -CONR¹²R¹³, SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl; or
- (g) Z-alkylene-NR³⁰R³¹ where Z is -NH-, -N(alkyl)- or -O-, and R³⁰ and R³¹ are independently of each other, hydrogen, alkyl or heteroalkyl.

22. (Amended Herein) The method of Claim 16, wherein R³ is heteroalkoxy.
23. (Amended Herein) The method of Claim 22, wherein R³ is at the 3-position and is selected from the group consisting of 3-dimethylaminopropoxy, 2-dimethylaminoethoxy, 2-hydroxyethoxy, 2,3-dihydroxypropoxy, and 2,2-(dihydroxymethyl)ethoxy.
24. The method of Claim 23 wherein R⁵ is 4-F or 2-Me and R⁶ is hydrogen.
25. The method of Claim 16, wherein R³ is optionally substituted heterocyclalkyl, optionally substituted heterocyclalkoxy or optionally substituted heterocyclalkylamino.
26. The method of Claim 25, wherein R³ is at the 3-position and is selected from the group consisting of 3-(morpholin-4-yl)propoxy, 2-(morpholin-4-yl)ethoxy, 2-(2-oxopyrrolidin-1-yl)ethoxy, 3-(morpholin-4-yl)propyl, 2-(morpholin-4-yl)ethyl, 4-(morpholin-4-yl)butyl, 3-(morpholin-4-yl)propylamino, 2-(morpholin-4-yl)ethylamino, 4-hydroxypiperidinylmethyl, 2-(S,S-dioxo-thiamorpholin-4-yl)ethyl, 3-(S,S-dioxo-thiamorpholin-4-yl)propyl and N-methylpiperazinylmethyl.
27. The method of Claim 26 wherein R⁵ is 4-F or 2-Me and R⁶ is hydrogen.
28. (Amended Herein) The method of Claim 16 wherein R³ is -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted

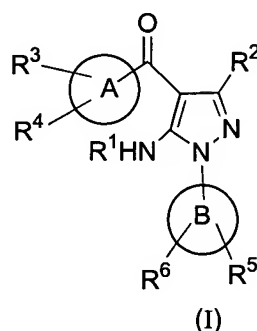
heteroaryl, $-\text{CONR}^{12}\text{R}^{13}$, $-\text{SO}_2\text{R}^{14}$, $-\text{SO}_2\text{NR}^{15}\text{R}^{16}$, $-\text{NHSO}_2\text{R}^{17}$ or $-\text{NHSO}_2\text{NR}^{18}\text{R}^{19}$ where R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl.

29. (Amended Herein) The method of Claim 28, wherein Y is a single bond and R^9 is $-\text{SO}_2\text{R}^{14}$ or $-\text{SO}_2\text{NR}^{15}\text{R}^{16}$.

30. The method of Claim 29 wherein R^3 is methylsulfonyl or sulfamoyl.

31. The method of Claim 30 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.

33. (Amended Herein) A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a therapeutically effective amount of a compound selected from the group of compounds represented by Formula (I):



wherein:

R^1 is hydrogen or acyl;

R^2 is hydrogen or alkyl;

A is an aryl ring;

B is an aryl ring;

R^3 is selected from the group consisting of:

- (a) acylamino;
- (b) optionally substituted heterocyclyl;
- (c) optionally substituted aryl or heteroaryl;

- (d) heteroalkenyl;
- (e) heteroalkynyl;
- (f) heteroalkoxy;
- (g) optionally substituted heterocyclalkyl;
- (h) optionally substituted heterocyclalkenyl;
- (i) optionally substituted heterocyclalkynyl;
- (j) optionally substituted heterocyclalkoxy, cycloxy, or heterocycloxy;
- (k) optionally substituted heterocyclalkylamino;
- (l) optionally substituted heterocyclalkylcarbonyl;
- (m) $\text{-NHSO}_2\text{R}^6$ where R^6 is optionally substituted heterocyclalkyl;
- (n) $\text{-NHSO}_2\text{NR}^7\text{R}^8$ where R^7 and R^8 are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (o) -Y-(alkylene)-R^9 where:
Y is a single bond, -O- , -NH- or $\text{-S(O)}_n\text{-}$ (where n is an integer from 0 to 2); and R^9 is cyano, optionally substituted heteroaryl, -COOH , -COR^{10} , -COOR^{11} , $\text{-CONR}^{12}\text{R}^{13}$, $\text{-SO}_2\text{R}^{14}$, $\text{-SO}_2\text{NR}^{15}\text{R}^{16}$, $\text{-NHSO}_2\text{R}^{17}$ or $\text{-NHSO}_2\text{NR}^{18}\text{R}^{19}$, where R^{10} is optionally substituted heterocycle, R^{11} is alkyl, and R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (p) $\text{-C(=NR}^{20}\text{)(NR}^{21}\text{R}^{22}\text{)}$ where R^{20} , R^{21} and R^{22} independently represent hydrogen, alkyl or hydroxy, or R^{20} and R^{21} together are $\text{-(CH}_2\text{)}_n\text{-}$ where n is 2 or 3 and R^{22} is hydrogen or alkyl;
- (q) $\text{-NHC(=X)NR}^{23}\text{R}^{24}$ where X is O or S, and R^{23} and R^{24} are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (r) $\text{-CONR}^{25}\text{R}^{26}$ where R^{25} and R^{26} independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclalkyl, or

R^{25} and R^{26} together with the nitrogen to which they are attached form an optionally substituted heterocyclyl ring;

- (s) $-S(O)_nR^{27}$ where n is an integer from 0 to 2, and R^{27} is optionally substituted heterocyclylalkyl;
- (t) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;
- (u) arylaminoalkylene or heteroarylaminoalkylene;
- (v) Z-alkylene- $NR^{30}R^{31}$ or Z-alkylene- OR^{32} where Z is -O-, and R^{30} , R^{31} and R^{32} are independently of each other, hydrogen, alkyl or heteroalkyl;
- (w) $-OC(O)$ -alkylene- CO_2H or $-OC(O)$ - $NR'R''$ (where R' and R'' are independently hydrogen or alkyl); and
- (x) heteroarylalkenylene or heteroarylalkynylene;

R^4 is selected from the group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) alkoxy; and
- (e) hydroxy;

R^5 is selected from the group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) haloalkyl;
- (e) thioalkyl;
- (f) hydroxy;
- (g) amino;
- (h) alkylamino;
- (i) dialkylamino;

- (j) heteroalkyl;
- (k) optionally substituted heterocycle;
- (l) optionally substituted heterocyclalkyl;
- (m) optionally substituted heterocyclalkoxy;
- (n) alkylsulfonyl;
- (o) aminosulfonyl, mono-alkylaminosulfonyl or dialkylaminosulfonyl;
- (p) heteroalkoxy; and
- (q) carboxy;

R⁶ is selected from a group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl; and
- (d) alkoxy; and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

34. The method of Claim 33 wherein the disease is an inflammatory disease.

35. The method of Claim 34 wherein the disease is arthritis.